

What is claimed is:

1. A method of identifying an acetyltransferase substrate in a sample, the method comprising combining the sample with

a labeled reagent comprising a thiol,

5 a halo-acetyl-CoA or a halo-acetyl-pantetheine, and

an acetyltransferase,

under conditions suitable for acetyltransferase enzyme activity, then identifying a substrate that has formed a base-stable covalent bond to the reagent.

10 2. The method of claim 1, wherein the labeled reagent is the halo-acetyl-CoA or halo-acetyl-pantetheine.

3. The method of claim 1, wherein the labeled reagent is not the halo-acetyl-CoA or halo-acetyl-pantetheine.

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4. The method of claim 3, wherein the labeled reagent is a thiol-containing fluorophore.

5. The method of claim 4, wherein the thiol-containing fluorophore is a fluorophore modified with aminoethanethiol.

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6. The method of claim 3, wherein the labeled reagent further comprises an oligo-His moiety.

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7. The method of claim 1, wherein the acetyltransferase is a prokaryotic acetyltransferase.

8. The method of claim 1, wherein the acetyltransferase is a eucaryotic acetyltransferase.

9. The method of claim 1, wherein the acetyltransferase is an archaeal acetyltransferase.

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10. The method of claim 1, wherein the acetyltransferase is selected from the group consisting of a histone acetyltransferase, an N-terminal acetyltransferase, an arylamine N-acetyltransferase, an aminoglycoside acetyltransferase, chloramphenicol acetyltransferase, choline acetyltransferase, carnitine acetyltransferase, spermine acetyltransferase, and ornithine acetyltransferase.

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11. The method of claim 1, wherein the halo-acetyl-CoA or halo-acetyl-pantetheine is a halo-acetyl-CoA.

5        12. The method of claim 11, wherein the halo-acetyl-CoA is a chloroacetyl-CoA or a bromoacetyl-CoA.

13. The method of claim 11, wherein the halo-acetyl-CoA is a fluoroacetyl-CoA or an iodoacetyl-CoA.

10        14. The method of claim 11, wherein the halo-acetyl-CoA is labeled on the adenine group of the CoA.

15. The method of claim 1, wherein the label is radioactive.

15        16. The method of claim 15, wherein the radioactive label is <sup>32</sup>P.

17. The method of claim 1, wherein the label is fluorescent.

20        18. The method of claim 1, wherein the label is an affinity label.

19. The method of claim 18, wherein the affinity label is biotin.

20        20. The method of claim 1, wherein the substrate is a protein.

25        21. The method of claim 1, wherein the substrate is an antibiotic.

22. The method of claim 1, wherein the substrate is a metabolite less than 500 molecular weight.

30        23. The method of claim 1, wherein the sample comprises an extract of a cell.

24. The method of claim 1, wherein the substrate is identified by methods comprising gel electrophoresis.

25. The method of claim 1, wherein the substrate is identified by methods comprising mass spectroscopy and/or nuclear magnetic resonance.

26. A method of identifying an acetyltransferase substrate in a sample, the method  
5 comprising combining the sample with a reagent and an acetyltransferase under conditions suitable for acetyltransferase enzyme activity, then identifying a substrate that is associated with the acetyltransferase,

wherein the reagent is a halo-acetyl-CoA or a halo-acetyl-pantetheine, and  
wherein the acetyltransferase further comprises an affinity tag.

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27. The method of claim 26, wherein the reagent is a halo-acetyl-CoA.

28. The method of claim 27, wherein the halo-acetyl-CoA is a chloroacetyl-CoA.

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29. The method of claim 27, wherein the halo-acetyl-CoA is a bromoacetyl-CoA.

30. The method of claim 27, wherein the halo-acetyl-CoA is an iodoacetyl-CoA or fluoroacetyl-CoA.

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31. The method of claim 26, wherein the affinity tag is an oligo-His tag.

32. A method of localizing acetylation of an acetyltransferase substrate in a cell, the method comprising combining the cell with

a labeled reagent comprising a thiol, and

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a halo-acetyl-CoA or a halo-acetyl-pantetheine,

under conditions suitable for acetyltransferase enzyme activity, then determining the location of the label in the cell.

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33. The method of claim 32, wherein the labeled reagent is the halo-acetyl-CoA or halo-acetyl-pantetheine.

34. The method of claim 32, wherein the labeled reagent is not the halo-acetyl-CoA or halo-acetyl-pantetheine.

35. The method of claim 34, wherein the labeled reagent is a thiol-containing fluorophore.

36. The method of claim 35, wherein the thiol-containing fluorophore is a fluorophore  
5 modified with aminoethanethiol.

37. The method of claim 32, wherein the label is radioactive.

38. The method of claim 37, wherein the radioactive label is  $^{32}\text{P}$ .

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39. The method of claim 32, wherein the label is fluorescent.

40. The method of claim 32, wherein the label is an affinity label.

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41. The method of claim 40, wherein the affinity label is biotin.

42. The method of claim 32, wherein the substrate is a histone.

43. The method of claim 32, wherein the location of the label in the cell is determined by  
20 light microscopy, autoradiography, or fluorescence microscopy.

44. The method of claim 32, wherein the cell is a eucaryotic cell.

45. The method of claim 32, wherein the cell is a prokaryotic cell.

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46. A method of labeling a substrate of an acetyltransferase, the method comprising  
combining the substrate with  
a labeled reagent comprising a thiol,  
a halo-acetyl-CoA or a halo-acetyl-pantetheine, and  
30 an acetyltransferase,  
under conditions suitable for acetyltransferase enzyme activity.

47. The method of claim 46, wherein the labeled reagent is the halo-acetyl-CoA or halo-  
acetyl-pantetheine.

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48. The method of claim 46, wherein the labeled reagent is not the halo-acetyl-CoA or halo-acetyl-pantetheine.

5       49. The method of claim 48, wherein the labeled reagent is a thiol-containing fluorophore.

50. The method of claim 49, wherein the thiol-containing fluorophore is a fluorophore modified with aminoethanethiol.

10       51. The method of claim 48, wherein the labeled reagent further comprises an oligo-His moiety.

15       52. The method of claim 46, wherein the acetyltransferase is selected from the group consisting of a histone acetyltransferase, an N-terminal acetyltransferase, an arylamine N-acetyltransferase, an aminoglycoside acetyltransferase, chloramphenicol acetyltransferase, choline acetyltransferase, carnitine acetyltransferase, spermine acetyltransferase, and ornithine acetyltransferase.

20       53. The method of claim 46, wherein the halo-acetyl-CoA or halo-acetyl-pantetheine is a halo-acetyl-CoA.

54. The method of claim 53, wherein the halo-acetyl-CoA is a chloroacetyl-CoA or bromoacetyl-CoA.

25       55. The method of claim 53, wherein the halo-acetyl-CoA is a fluoroacetyl-CoA or an iodoacetyl-CoA.

56. The method of claim 53, wherein the halo-acetyl-CoA is labeled on the adenine group of the CoA.

30       57. The method of claim 46, wherein the label is radioactive.

58. The method of claim 57, wherein the radioactive label is  $^{32}\text{P}$ .

35       59. The method of claim 46, wherein the label is fluorescent.

60. The method of claim 46, wherein the label is an affinity label.

61. The method of claim 60, wherein the affinity label is biotin.

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62. The method of claim 46, wherein the substrate is in a cellular extract.

63. A method of assaying an acetyltransferase in a sample, the method comprising combining the sample with

10 a labeled reagent comprising a thiol,

a halo-acetyl-CoA or a halo-acetyl-pantetheine, and

an acetyltransferase substrate

under conditions suitable for acetyltransferase enzyme activity, then determining whether the substrate has formed a base-stable covalent bond to the reagent,

15 wherein the presence of the base-stable bond of the reagent to the substrate indicates the presence of an acetyltransferase in the sample.

64. The method of claim 63, wherein the labeled reagent is the halo-acetyl-CoA or halo-acetyl-pantetheine.

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65. The method of claim 63, wherein the labeled reagent is not the halo-acetyl-CoA or halo-acetyl-pantetheine.

25 66. The method of claim 65, wherein the labeled reagent is a thiol-containing fluorophore.

67. The method of claim 66, wherein the thiol-containing fluorophore is a fluorophore modified with aminoethanethiol.

30 68. The method of claim 65, wherein the labeled reagent further comprises an oligo-His moiety.

69. The method of claim 63, wherein the sample comprises an extract of a cell.

35 70. The method of claim 69, wherein the cell is a prokaryotic cell or an archaeal cell.

71. The method of claim 69, wherein the cell is a eucaryotic cell.

72. The method of claim 63, wherein the halo-acetyl-CoA or halo-acetyl-pantetheine is a  
5 halo-acetyl-CoA.

73. The method of claim 72, wherein the halo-acetyl-CoA is a chloroacetyl-CoA or a  
bromoacetyl-CoA.

10 74. The method of claim 72, wherein the halo-acetyl-CoA is a fluoroacetyl-CoA or an  
iodoacetyl-CoA.

75. The method of claim 72, wherein the halo-acetyl-CoA is labeled on the adenine  
group of the CoA.

15 76. The method of claim 63, wherein the label is radioactive.

77. The method of claim 76, wherein the radioactive label is <sup>32</sup>P.

20 78. The method of claim 63, wherein the label is fluorescent.

79. The method of claim 63, wherein the substrate is a protein.

80. The method of claim 79, wherein the protein is a histone.

25 81. The method of claim 63, wherein the substrate is an antibiotic.

82. The method of claim 63, wherein the substrate is a metabolite less than 500  
molecular weight.

30 83. A method of quantifying acetyltransferase activity in a sample, the method  
comprising combining the sample with  
a labeled reagent comprising a thiol,  
a halo-acetyl-CoA or a halo-acetyl-pantetheine, and  
35 an acetyltransferase substrate,

under conditions suitable for acetyltransferase enzyme activity, then quantifying the labeled reagent that has formed a base-stable covalent bond to the substrate,

wherein the quantity of labeled reagent that has formed a base-stable covalent bond to the substrate is proportional to the acetyltransferase activity in the sample.

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84. The method of claim 83, wherein the labeled reagent is the halo-acetyl-CoA or halo-acetyl-pantetheine.

10 85. The method of claim 83, wherein the labeled reagent is not the halo-acetyl-CoA or halo-acetyl-pantetheine.

86. The method of claim 85, wherein the labeled reagent is a thiol-containing fluorophore.

15 87. The method of claim 86, wherein the thiol-containing fluorophore is a fluorophore modified with aminoethanethiol.

88. The method of claim 85, wherein the labeled reagent further comprises an oligo-His moiety.

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89. The method of claim 83, wherein the sample comprises an extract of a cell.

90. The method of claim 89, wherein the cell is a prokaryotic cell or an archaeal cell.

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91. The method of claim 89, wherein the cell is a eucaryotic cell.

92. The method of claim 83, wherein the halo-acetyl-CoA or halo-acetyl-pantetheine is a halo-acetyl-CoA.

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93. The method of claim 92, wherein the halo-acetyl-CoA is a chloroacetyl-CoA or a bromoacetyl-CoA.

94. The method of claim 92, wherein the halo-acetyl-CoA is a fluoroacetyl-CoA or an iodoacetyl-CoA.

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95. The method of claim 92, wherein the halo-acetyl-CoA is labeled on the adenine group of the CoA.

96. The method of claim 83, wherein the label is radioactive.

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97. The method of claim 96, wherein the radioactive label is  $^{32}\text{P}$ .

98. The method of claim 83, wherein the label is fluorescent.

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99. The method of claim 83, wherein the substrate is a protein.

100. The method of claim 99, wherein the protein is a histone.

101. The method of claim 83, wherein the substrate is an antibiotic.

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102. The method of claim 83, wherein the substrate is a metabolite less than 500 molecular weight.

103. A halo-acetyl-pantetheine.

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104. The halo-acetyl-pantetheine of claim 103, wherein the halo group is a chloro- or bromo-.

105. The halo-acetyl-pantetheine of claim 103, wherein the halo group is a fluoro- or an

25 iodo-.

106. A halo-acetyl-pantetheine with a label, wherein the label is a detectable label or an affinity label.

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107. The halo-acetyl-pantetheine of claim 106, wherein the label is a radioactive label.

108. The halo-acetyl-pantetheine of claim 107, wherein the radioactive label is  $^{32}\text{P}$  or  $^{14}\text{C}$ .

109. The halo-acetyl-pantetheine of claim 106, wherein the label is a fluorescent label.

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110. The halo-acetyl-pantetheine of claim 106, wherein the label is biotin.

111. A halo-acetyl-CoA labeled with  $^{32}\text{P}$ , a fluorescent label, or an affinity label.

5 112. The halo-acetyl-CoA of claim 111, wherein the halo group is a chloro- or a bromo-.

113. The halo-acetyl-CoA of claim 111, wherein the halo group is a fluoro- or an iodo-.

114. The halo-acetyl-CoA of claim 111, wherein the label is biotin.

10 115. A halo-acetyl-CoA with a label on the adenine of the CoA, wherein the label is a detectable label or an affinity label.

116. The halo-acetyl-CoA of claim 115, wherein the label is a radioactive label.

15 117. The halo-acetyl-CoA of claim 116, wherein the radioactive label is  $^{32}\text{P}$ .

118. The halo-acetyl-CoA of claim 115, wherein the label is a fluorescent label.

20 119. The halo-acetyl-CoA of claim 115, wherein the label is biotin.

120. A compound comprising an oligo-His moiety, a thiol, and a detectable label.

121. The compound of claim 120, wherein the detectable label is a fluorescent label.

25 122. The compound of claim 120, wherein the compound is an acetyltransferase substrate.